

CLAIMS

1. A conjugate having the following structure

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$$\begin{array}{c} \text{CO- L}_B\text{-NH-P-CO-Y} \\ X\text{-L}_A\text{- R} < \\ \text{CO- L}_B\text{-NH-P-CO-Y} \end{array}$$

wherein

10 R represents $-\text{N}(\text{CH}_2)^2$, $-\text{NHCH}^<$ or $-\text{NHCH}(\text{CH}_2)^2$,
X represents a hydrogen or a peptidic group, and
 L_A is optionally present and is an amino acid or a peptide containing at least 2 amino acid residues,

15 L_B is optionally present and is an amino acid or a peptide containing at least 2 amino acid residues,

P is a peptide selected from full length or fragments of amyloid proteins or proteins with substantial similarity to an amyloid protein,

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and pharmaceutically acceptable salts thereof.

25 2. A conjugate according to claim 1, which upon administration to a mammal is capable of eliciting a production of antibodies having specificity towards the conjugate itself, and inducing an immune response in the mammal, thereby preventing or reducing amyloid-induced cellular toxicity and/or the formation of amyloid fibrils, plaques and/or deposits.

30 3. A conjugate according to claim 2, wherein the antibodies produced are having specificity towards one or more C-terminally presented P peptides of the conjugate.

4. A conjugate according to any of claims 1-3, wherein P is a fragment comprising at least one region of an amyloid protein.

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5. A conjugate according to claim 4, wherein the region is selected from the group comprising the C-terminal region, beta sheet region, cytotoxic region, GAG-binding site region, or macrophage adherence region.

6. A conjugate according to any of the preceding claims, wherein the amyloid proteins are derived from amyloid precursor proteins selected from the group comprising serum amyloid A protein (ApoSSA), immunoglobulin light chain, immunoglobulin heavy chain, ApoA1, transthyretin, lysozyme, fibrinogen alpha chain, gelsolin, cystatin C, amyloid

5 beta protein precursor (beta.-APP), beta₂ microglobulin, prion precursor protein (PrP), atrial natriuretic factor, keratin, islet amyloid polypeptide and synuclein or any polypeptides with substantial similarity to any of the above.

7. A conjugate according to any of claims 1-5, wherein the amyloid proteins are

10 selected from amyloid beta (1-43), amyloid beta (1-42), amyloid beta (1-41), amyloid beta (1-40), amyloid beta (1-39) and amyloid beta (1-38).

8. A conjugate according to claim 7, wherein P is a fragment of amyloid beta (1-43),

15 amyloid beta (1-42), amyloid beta (1-41), amyloid beta (1-40), amyloid beta (1-39) or amyloid beta (1-38).

9. A conjugate according to claim 8, wherein P contains the C-terminus of amyloid

beta.

20 10. A conjugate according to claim 8, wherein P is a fragment of 10 amino acids from the C-terminus of amyloid beta.

11. A conjugate according to claim 8, wherein P is a fragment of 9 amino acids from the C-terminus of amyloid beta.

25 12. A conjugate according to claim 8, wherein P is a fragment of 8 amino acids from the C-terminus of amyloid beta.

13. A conjugate according to claim 8, wherein P is a fragment of 7 amino acids from 30 the C-terminus of amyloid beta.

14. A conjugate according to claim 8, wherein P is a fragment of 6 amino acids from the C-terminus of amyloid beta.

35 15. A conjugate according to claim 8, wherein P is a fragment of 5 amino acids from the C-terminus of amyloid beta.

16. A conjugate according to claim 8, wherein P is a fragment of 4 amino acids from the C-terminus of amyloid beta.
17. A conjugate according to claim 8, wherein P is a fragment of 3 amino acids from 5 the C-terminus of amyloid beta.
18. A conjugate according to claim 12, wherein P is fragment 35-42 of amyloid beta (1-42).
- 10 19. A conjugate according to claim 13, wherein P is fragment 36-42 of amyloid beta (1-42).
20. A conjugate according to claim 14, wherein P is fragment 37-42 of amyloid beta (1-42).
- 15 21. A conjugate according to claim 15, wherein P is fragment 38-42 of amyloid beta (1-42).
22. A conjugate according to claim 16, wherein P is fragment 39-42 of amyloid beta (1-42).
- 20 23. A conjugate according to claim 17, wherein P is fragment 40-42 of amyloid beta (1-42).
- 25 24. A conjugate according to any of the preceding claims, wherein X is a T cell epitope.
25. A conjugate according to claim 24, wherein X is a human T cell epitope including full-length tetanus toxoid, tetanus toxoid fragment FNNFTVSFWLRVPKVSASHLE and tetanus toxoid fragment YNDMFNNFTVSFWLRVPKVSASHLEQYGT, or a rodent T cell 30 epitope including QYIKANSKFIGITEL.
26. A conjugate according to any of claims 1-23, wherein X is Keyhole Limpet Hemocyanin or BSA.
- 35 27. A method for the treatment, amelioration and/or prophylaxis of an amyloid-related disease in a mammal, the method comprising administering to the mammal an

antigenic amount of a conjugate as defined in any of the claims 1-26, wherein the conjugate elicits the production of antibodies having specificity towards the conjugate itself and induces an immune response in the mammal, thereby preventing or reducing amyloid-induced cellular toxicity and/or the formation of fibrils, plaques and/or amyloid deposits.

28. A method according to claim 27, wherein the antibodies produced are being specific towards one or more C-terminally presented P peptides of a conjugate as defined in claims 1-26.

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29. A method according to claim 27 or 28, the method further comprises the administration of an adjuvant together with the conjugate.

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30. A method according to claim 29, wherein the adjuvant is selected from the group comprising complete Freunds adjuvant, incomplete Freunds adjuvant, QS21, Aluminium hydroxide gel, MF59 and calcium phosphate.

31. A method according to any of claims 27-30, wherein the amyloid-related disease is Alzheimer's disease, Down's syndrome, vascular dementia or cognitive impairment.

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32. Use of a conjugate as defined in any of claims 1-26 for the preparation of a pharmaceutical composition for the treatment and/or prophylaxis of an amyloid-related disease in a mammal.

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33. A vaccine comprising a conjugate as defined in claims 1-26 together with an adjuvant.

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34. A vaccine according to claim 33, wherein the adjuvant is selected from the group comprising complete Freunds adjuvant, incomplete Freunds adjuvant, QS21, Aluminium hydroxide gel, MF59 and calcium phosphate.

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35. A method for producing an antibody in a mammal, the method comprising administering to the mammal an antigenic amount of a conjugate as defined in any of the claims 1-26, wherein the conjugate elicits the production of antibodies having specificity towards the conjugate itself.

36. A method according to claim 35, wherein antibodies produced are being specific towards one or more C-terminally presented P peptides of a conjugate as defined in claims 1-26.

5 37. A method according to claim 35 or 36, which further comprises the step of generating hybridoma cells by somatic cell hybridization for the production of monoclonal or polyclonal antibodies.

10 38. A method according to any of claims 35-37, wherein the mammal is a mouse or humanized mouse.

39. An antibody having specificity towards a conjugate as defined in claims 1-26.

15 40. An antibody having specificity towards one or more C-terminally presented P peptides in a conjugate as defined in any of claims 1-26.

41. An antibody according to claim 39 or 40, which is monoclonal.

20 42. An antibody according to any of claims 39-41, which is humanized or chimeric.

43. An antibody according to any of claims 39-42, which is produced by a method as defined in claims 35-48.

25 44. A method for the treatment and/or prophylaxis of an amyloid-related disease in a mammal, the method comprising administering to the mammal an antibody as defined in claims 39-43, thereby preventing or reducing amyloid-induced cellular toxicity and/or the formation of fibrils, plaques and/or amyloid deposits.

30 45. A method according to claim 44, wherein the amyloid-related disease is Alzheimer's disease, Down's syndrome, vascular dementia or cognitive impairment.